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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/116,502 07/16/98 FALLON

R CL-1035

HM12/0804

EXAMINER

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WAX, R

ART UNIT	PAPER NUMBER
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1652

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DATE MAILED:

08/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/116,502	Applicant(s) Fallon et al.
	Examiner Robert A. Wax	Group Art Unit 1652

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 1-27 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 1-27 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 4 and 7

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statements

2. The information disclosure statements filed July 16, 1998, February 16, 1999 and May 5, 1999 have been considered. Please see the attached PTO-1449s.

Claim Objections

3. Claim 8 part b is objected to because of the following informalities: the claim recites "C22" rather than "C₂₂". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 4, 9, 11, 12, 20 and 26 are rejected under 35 U.S.C. 112, first paragraph, as improperly incorporating essential material by reference. The specification at least

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on page 17 and probably elsewhere refers to accession numbers for disclosure of the sequences of Alk1A, for example. This is essential material because one practicing the invention of the above claims would need to have access to the actual sequences of the components to be placed in the plasmids for expression. Correction is required via addition of the sequences to the disclosure. Applicants are reminded that when adding sequence the sequence rules must be followed (37 CFR 1.821-825).

5. Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 24 is directed to all possible DNA fragments comprising at least two *Candida maltosa* promoters and at least two *Candida maltosa* proteins. The claim reads on each chromosome of *Candida maltosa* less one nucleotide. While the specification mentions some *Candida maltosa* promoters and some *Candida maltosa* proteins there is no disclosure of a representative number of *Candida maltosa* promoters or a representative number of *Candida maltosa* proteins. There is no particular structure to function/activity relationship disclosed for a representative number of *Candida maltosa* promoters nor is there any disclosed for a representative number of *Candida maltosa* proteins. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe

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the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize Applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 10, 11 and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Park et al.

Park et al. teach simultaneous overexpression of ALK1 under the control of both GAL1 and GAL10 promoters on a single plasmid (see page 26 right column, final paragraph through page 27, left column, first paragraph. They use *Candida maltosa* as the host cell (see page 25, right column, last paragraph). Claims 10 and 24 are clearly anticipated by these teachings. Claim 11 is included because even though the specific accession numbers are not recited the ALK genes must be the same since they are *C. maltosa* genes.

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8. Claim 16 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Masuda et al.

Masuda et al. teach a transformed *Candida maltosa* which has both the POX2 and the POX4 genes disrupted, see Summary. This clearly anticipates claim 16.

9. Claims 24-26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Zimmer et al.

Zimmer et al. teach an expression vector containing both the *Candida maltosa* cytochromes P450 and NADPH-cytochrome P450 reductase for expression in *S. cerevisiae*. This clearly anticipates the above claims.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cregg et al. in view of Zimmer et al.

Cregg et al. teach how to express foreign genes in *Pichia pastoris* and the advantages of using *Pichia pastoris* as a host cell.

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The teachings of Zimmer et al. are outlined above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to place the expression vector of Zimmer et al. in *Pichia pastoris* as the host cell with the expectation of attaining the benefits taught by Cregg et al. Selection of specific *Candida maltosa* P450 monooxygenases and P450 reductases is deemed to be within the ordinary level of skill in the art since all of them appear to be equivalent.

12. Claims 8-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Picataggio et al. (5,254,466) in view of Picataggio et al. (1992), Masuda et al., Zimmer et al. and Schunck et al. (1989).

Picataggio et al. ('466) teach enhancement of long-chain mono and dicarboxylic acids by disruption of the β -oxidation pathway in *Candida tropicalis* by disruption of the POX4 genes. Use of the URA3 selectable marker is taught at figure 1A, for example.

Picataggio et al. (1992) teach enhanced production of long-chain dicarboxylic acids by transformation of *Candida tropicalis* host cells that have had their β -oxidation pathway blocked with genes encoding cytochrome P450 monooxygenase and P450 reductase (see page 894, right column, second paragraph). Basically, Picataggio et al. did exactly what the present inventors have done in *Candida maltosa* except in *Candida tropicalis*.

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As stated above, Masuda et al. teach disruption of the POX4 and POX2 genes in *Candida maltosa*. Another way of saying this is that Masuda et al. did the same thing in *Candida maltosa* that Picataggio et al. did in *Candida tropicalis*.

The teachings of Zimmer et al. are outlined above.

Schunck et al. (1989) provide the sequence of the alkane hydroxylating cytochrome P-450 of *Candida maltosa* and discuss the similarity between *Candida maltosa* and *Candida tropicalis*.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to enhance production of long chain mono and dicarboxylic acids in *Candida maltosa* by following the guidance provided by Picataggio et al. (1992) with the expectation of achieving the same results that they did in *Candida tropicalis*.

Motivation to select *Candida maltosa* as the host species is provided by Zimmer et al. in their Introduction where they state that the P450 forms "probably developed in adaptation of the microorganism to the utilization of different hydrocarbons." One of ordinary skill in the art would clearly select the organism most specifically adapted to product the desired protein. The expectation of success in using *Candida maltosa* as the host cell is provided by Schunck et al. (1989) who teach the similarity of *Candida maltosa* to *Candida tropicalis*. Selection of the specific substrates and enzymes of the claims is deemed to be within the ordinary level of skill in the art; claims reciting these limitations are thus considered to have been obvious as well. With regard to claim 27,

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the specific plasmids are considered to have been obvious in view of the teachings of coexpression of P450 monooxygenase with P450 reductase.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (703) 308-4216. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy, can be reached on (703) 308-3804. The OFFICIAL fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Robert A. Wax
Primary Examiner
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